



## Complete Summary

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### GUIDELINE TITLE

Stereotactic radiosurgery for patients with intracranial arteriovenous malformations (AVM).

### BIBLIOGRAPHIC SOURCE(S)

IRSA. Stereotactic radiosurgery for patients with intracranial arteriovenous malformations (AVM). Harrisburg (PA): IRSA; 2003 Sep. 10 p. (Radiosurgery Practice Guideline Report; no. 2-03). [46 references]

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## SCOPE

### DISEASE/CONDITION(S)

Arteriovenous malformations of the brain

### GUIDELINE CATEGORY

Management  
Treatment

### CLINICAL SPECIALTY

Neurological Surgery  
Neurology  
Radiation Oncology

### INTENDED USERS

Health Care Providers  
Hospitals  
Managed Care Organizations  
Nurses  
Physicians  
Utilization Management

#### GUIDELINE OBJECTIVE(S)

To provide guidelines about the use of stereotactic radiosurgery in symptomatic patients with imaging identified arteriovenous malformations of the brain

#### TARGET POPULATION

Men and women >2 years old with imaging identified congenital or acquired arteriovenous malformations of the brain, including the cerebrum, cerebellum, brainstem, and dura.

Note: Patients often are not considered candidates for surgical resection based on size or anatomic location, or medical co-morbidities and advanced age.

#### INTERVENTIONS AND PRACTICES CONSIDERED

1. Stereotactic radiosurgery
  - Intraoperative stereotactic guidance
  - Digitally acquired images (computed tomography [CT] or magnetic resonance imaging [MRI])
  - Intracranial angiography
2. Methylprednisolone treatment

#### MAJOR OUTCOMES CONSIDERED

Total obliteration of the arteriovenous malformation within three years is the primary end point of interest. Additional outcome end points include resolution or an improvement in seizure disorders if present, resolution or reduction in vascular headache syndromes, and prevention of bleeding risks from the arteriovenous malformation (estimated to vary between 1–10% per year depending upon prior bleeding history, location, and volume). Improvement in the existing neurological deficits is also considered. Maintenance of quality of life, employability, and prevention of adverse radiation effects are also considered.

### METHODOLOGY

#### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
Hand-searches of Published Literature (Secondary Sources)  
Searches of Electronic Databases

#### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

MEDLINE and PUBMED searches were completed for the years 1971 to September 2003. Search terms included arteriovenous malformation, AVM, vascular malformation, stereotactic radiosurgery, Gamma Knife®, irradiation, Linac radiosurgery, proton beam radiosurgery, Bragg peak proton therapy, clinical trials, research design, practice guidelines and meta-analysis. Bibliographies from recently published reviews were reviewed and relevant articles were retrieved.

## NUMBER OF SOURCE DOCUMENTS

46

## METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)  
Weighting According to a Rating Scheme (Scheme Given)

## RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

This classification is based on the Bandolier system (<http://www.jr2.ox.ac.uk/bandoiler/band6/b6-5.html>) adapted for a systematic review.

### Type & Strength of Evidence in Medical Literature

Type I: Evidence from a systematic review (which includes at least one randomized controlled trial and a summary of all included studies).

Type II: Evidence from a well designed randomized controlled trial of appropriate size.

Type III: Evidence from a well designed intervention study without randomization. A common research design is the before-and-after study.

Type IV: Evidence from a well designed non-experimental study, e.g., cohort, case-control or cross-sectional studies. (Also includes studies using purely qualitative methods. Economic analyses [cost-effectiveness studies] are also classified as Type IV evidence.)

Type V: Opinions of respected authorities, based on clinical evidence, descriptive studies or reports of expert consensus committees.

## METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses  
Systematic Review with Evidence Tables

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The initial draft of the consensus statement was a synthesis of research information obtained in the evidence-gathering process. The recommendations were originally suggested by a core group of four members of the working group. The recommendations were mailed to all committee members. Feedback was obtained through this mailed survey in order to revise the proposed guidelines. Committee members were asked whether the recommendations should serve as a practice guideline. No significant disagreements existed.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

External Peer Review  
Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The final statement incorporates all relevant evidence obtained by the literature search in conjunction with the final consensus recommendations supported by all working group members. The guideline was approved by the IRSA (International RadioSurgery Association) Board of Directors and issued in September 2003.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Stereotactic radiosurgery is defined as a relatively high dose of focused radiation delivered precisely to the arteriovenous malformations (AVM), under the direct supervision of a medical team (neurosurgeon, radiation oncologist, registered nurse, and medical physicist), in one surgical session.

#### Patient Selection

- Patients with intracranial AVM defined by modern neurodiagnostic imaging, including computed tomography (CT), magnetic resonance imaging (MRI) scan, and cerebral angiography, should be considered for radiosurgery. Such

patients typically present with brain hemorrhage (especially when located in deep anatomic locations of the brain), persistent seizures, vascular headache syndrome, or progressive neurological deficits.

- The selection of patients suitable for radiosurgery is dependent on the prior bleeding history, the age of the patient, existing co-morbidities, anatomic location, and clinical history.

## Treatment/Management

- Arteriovenous malformations are considered suitable for four management strategies alone or in combination: observation only, surgical excision, endovascular embolization (designed to reduce either a selected volume or flow through the AVM), and stereotactic radiosurgery.
- Stereotactic radiosurgery is typically employed alone but also may be employed in combination with prior surgery or embolization in particular circumstances. Size ranges of average diameter are usually less than 3 cm ( $0.1 - 10 \text{ cm}^3$ ). Prospective stereotactic radiosurgery volumetric staging is frequently performed for those symptomatic patients with AVM volumes  $>15 \text{ cm}^3$  in the absence of other acceptable risk management strategies and can be considered for AVMs between 10 to  $15 \text{ cm}^3$ .
- The optimal dose range for volumetric conformal stereotactic AVM radiosurgery has been largely established based on location and volume of the AVM. Doses at the margin of the AVM typically range from 16 to 25 Gy in a single fraction, wherein the volume of the AVM is defined by stereotactic guidance during the procedure itself. Stereotactic volumetric axial plane imaging (MRI or CT) supplemented by conventional or digital subtraction angiography is usually necessary for complete conformal dose planning.
- Dose selection depends on location, volume, estimated adverse radiation risks, pre-existing neurological conditions, and prior bleeding history. Depending upon the technology used, the margin of the AVM dose is usually 50 to 70% of the central target dose within the AVM. Sharp fall-off of the radiation dose outside of the target volume is required. Current radiation delivery technologies for volumetric stereotactic conformal single fraction radiosurgery include Gamma Knife®, proton beam using Bragg peak effect, and specially modified linear accelerators.
- Patients usually receive a single dose (40 mg) of methylprednisolone at the conclusion of the radiosurgery procedure. They can continue to take their other medications (e.g., antiepileptics, analgesics) during and after the procedure as recommended by their physicians.
- Some AVM patients will have been previously treated by embolization for volumetric reduction or flow reduction. Some patients may have had prior intracranial surgery for blood clot (hematoma) evacuation or partial AVM resection. The safe interval between surgery and stereotactic radiosurgery is not known, but it is reasonable to perform radiosurgery once the patient has achieved a stable neurological recovery or plateau (generally within two to three months after the intracranial hemorrhage or prior surgery). The optimal time between prior embolization and radiosurgery is not known, but generally waiting for a period of several weeks is considered beneficial in order to reduce the likelihood of vascular ischemic complications or residual cerebral edema sometimes associated with embolization followed by early radiosurgery.

- Postradiosurgical clinical examinations and magnetic resonance (MR) studies are requested by referring physicians at six-month intervals for the first three years to assess the effect of radiosurgery on AVM (gradual obliteration). If MR at the three-year mark suggests complete disappearance of the AVM nidus, an angiogram is obtained to confirm the obliteration. If the MR imaging before three years suggests nidus obliteration, angiography is generally delayed until three full years have elapsed. If angiography after three years demonstrates that the AVM nidus is not obliterated, repeat stereotactic radiosurgery is recommended.
- Patients who have residual arteriovenous malformations identified by neurodiagnostic imaging at three years (after radiosurgery) may be candidates for a second stereotactic radiosurgical procedure. Alternatively, patients with larger volume AVMs (e.g.,  $>10 \text{ cm}^3$ ) may be considered suitable for up-front volumetric staging of AVMs by treating different anatomic components of the AVM at intervals staged between three and six months. The interval for staging of radiosurgery prospectively is not established. Stereotactic radiosurgery should not be considered as the panacea for large volume AVMs unsuitable for surgery or embolization. At selected centers with experience, estimated obliteration rates after two radiosurgical procedures at five years approach 60 to 70%. For smaller volume AVMs (e.g., average diameters  $<3 \text{ cm}^3$ ), estimated complete obliteration rates at three years after a single procedure vary from 70 to 90%.
- Causes for failure of stereotactic radiosurgery have been identified and include inadequate visualization of the target nidus, lack of intraoperative stereotactic 3-D (volumetric axial plane imaging), insufficient dose to achieve the oblitative response, compression of the AVM nidus by a prior hematoma, or poor nidus visualization secondary to overlying vascular structures. In a few cases, selected radiobiological resistance of undetermined etiology may be the cause of obliteration failure.
- At present, technologies delivered to provide volumetric stereotactic radiosurgery are limited to Gamma Knife®, modified linear accelerators at centers supplemented by significant experience, and proton beam facilities in the United States.

## CLINICAL ALGORITHM(S)

The original guideline contains a clinical algorithm for arteriovenous malformation management.

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Type I, II, and III evidence exists in support of stereotactic radiosurgery for arteriovenous malformations (AVMs). Refer to the "Rating Scheme for the Strength of the Evidence" field.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- All the published studies have shown a significant response of stereotactic radiosurgery for arteriovenous malformations (AVMs) including a high rate of AVM nidus obliteration, concomitant improvement in seizure control, headache resolution, and a satisfactory (low) rate of adverse radiation effect that might lead to additional neurological deficits.
- Potential successful outcomes include complete AVM obliteration, symptomatic relief, no new neurological deficits, no long-term complications, and life-long prevention of bleeding risks.
- Literature has documented the cost savings benefit of stereotactic radiosurgery versus invasive surgical procedures and the lower risk potential of bleeding, anesthesia problems, infections, and side effects which may result in transient or permanent disabilities from open surgery.

#### Subgroups Most Likely to Benefit:

Radiosurgery, a minimally invasive closed skull treatment strategy, may be especially suitable for patients in advanced age groups or those with excessive medical co-morbidity risk factors for surgical excision and for those with malformations located in eloquent areas of the brain that open surgery would likely result in severe neurological deficits.

#### POTENTIAL HARMS

Major adverse effects of radiosurgery are based on location, volume, dose, and flow, and these risks can be estimated based on published data and experience. Individual risks are related to the anatomical location of the arteriovenous malformation (AVM). Currently, the estimated adverse risk of permanent new neurological deficits related to radiation in a large group of patients undergoing radiosurgery is 3 to 5%. Late delayed potential risks of radiosurgery should be assessed by magnetic resonance imaging (MRI) at five and ten years after obliteration is confirmed.

#### Subgroups Most Likely to be Harmed:

- Patients with large volume AVMs who are treated with large doses in a single fraction, especially if the AVM is located in a deep brain area
- Patients with large AVMs in a deep brain area, in whom the risk of bleeding over their expected lifetime is less than the risk of radiosurgery complications

### CONTRAINDICATIONS

#### CONTRAINDICATIONS

Patients with small volume ( $<10 \text{ cm}^3$ ), lobar location malformations that can be easily removed or resected without permanent neurological deficits.

### QUALIFYING STATEMENTS

#### QUALIFYING STATEMENTS

- This guideline is intended to provide the scientific foundation and initial framework for the person who has been diagnosed with a brain or dural arteriovenous malformation. The assessment and recommendations provided herein represent the best professional judgment of the working group at this time, based on research data and expertise currently available. The conclusions and recommendations will be regularly reassessed as new information becomes available.
- Complete obliteration of the arteriovenous malformation (AVM) is considered necessary in order to definitely eliminate the risk of future bleeding. To date, insufficient evidence exists to establish whether bleeding rates are reduced more than five years after AVM radiosurgery even in patients who have had incomplete obliteration.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Living with Illness

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

IRSA. Stereotactic radiosurgery for patients with intracranial arteriovenous malformations (AVM). Harrisburg (PA): IRSA; 2003 Sep. 10 p. (Radiosurgery Practice Guideline Report; no. 2-03). [46 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2003 Sep

### GUIDELINE DEVELOPER(S)



IRSA - Professional Association

#### GUIDELINE DEVELOPER COMMENT

IRSA (International RadioSurgery Association) is a non-profit entity dedicated to promoting the development of scientifically relevant practice guidelines for stereotactic radiosurgery. IRSA works to educate and provide support for physicians, hospitals, insurers, and patients.

#### SOURCE(S) OF FUNDING

IRSA (International RadioSurgery Association)

#### GUIDELINE COMMITTEE

IRSA (International RadioSurgery Association) Physician Advisory Board Guidelines Committee and other professionals who provide radiosurgery

#### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: L. Dade Lunsford, MD, Neurosurgeon, (Chair); Douglas Kondziolka, MD, Neurosurgeon; Ajay Niranjana, MBBS, MCh, Neurosurgeon; Christer Lindquist, MD, Neurosurgeon (European Co-Chair); Jay Loeffler, MD, Radiation Oncologist; Michael McDermott, MD, Neurosurgeon; Michael Sisti, MD, Neurosurgeon; John C. Flickinger, MD, Radiation Oncologist; Ann Maitz, MS, Medical Physicist; Michael Horowitz, MD, Neurosurgeon and Interventional Radiologist; Tonya K. Ledbetter, MS, MFS, Editor; Rebecca L. Emerick, MS, MBA, CPA, ex officio

#### FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

#### GUIDELINE STATUS

This is the current release of the guideline.

#### GUIDELINE AVAILABILITY

Electronic copies: Available from the [IRSA Web site](#).

Print copies: Available from the IRSA (International RadioSurgery Association), 3005 Hoffman Street, Harrisburg, PA 17110

#### AVAILABILITY OF COMPANION DOCUMENTS

None available

#### PATIENT RESOURCES

The following are available:

- Intracranial arteriovenous malformations & stereotactic radiosurgery. Harrisburg (PA): IRSA. 2003.
- AVMs. Brain Talk 2003;8(2):1-8. Electronic copies: Available in Portable Document Format (PDF) from the [IRSA Web site](#).
- AVMs. Another Perspective 1998;3(1):1-12.
- Neurosurgical radiosurgery. Brain Talk 2001;6(1):1-12. Electronic copies: Available in Portable Document Format (PDF) from the [IRSA Web site](#).
- Radiosurgery & radiation therapy overview. Another Perspective 1999;4(2):1-12. Electronic copies: Available in Portable Document Format (PDF) from the [IRSA Web site](#).

Print copies: Available from the IRSA, 3005 Hoffman Street, Harrisburg, PA 17110.

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## NGC STATUS

This NGC summary was completed by ECRI on March 8, 2004. The information was verified by the guideline developer on April 7, 2004.

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